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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.												
10/620,796	07/16/2003	Jack E. Tabaska	38-21(52529)B	3342												
7590 Pamela J. Sisson Patent Department E2NA, Monsanto Company 800 N. Lindbergh Blvd. St. Louis, MO 63167		06/25/2007	<table border="1"><tr><td colspan="2">EXAMINER</td></tr><tr><td colspan="2">WHALEY, PABLO S</td></tr><tr><td>ART UNIT</td><td>PAPER NUMBER</td></tr><tr><td>1631</td><td></td></tr><tr><td>MAIL DATE</td><td>DELIVERY MODE</td></tr><tr><td>06/25/2007</td><td>PAPER</td></tr></table>		EXAMINER		WHALEY, PABLO S		ART UNIT	PAPER NUMBER	1631		MAIL DATE	DELIVERY MODE	06/25/2007	PAPER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/620,796

Applicant(s)

TABASKA, JACK

Examiner

Pablo Whaley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' remarks, filed 01/29/2007, have been fully considered. The following rejections and/or objections are either withdrawn, maintained, or newly applied, as necessitated by amendment, for the reasons set forth below. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims 1-5 are herein under examination. The species elections for Specie I, II, and III, elected by applicant in the reply filed on 3/1/06, are hereby withdrawn as the Examiner has determined that they are not deemed to be a search burden.

PETITION

Applicant's petition for revival was reviewed by the Office of Petitions and granted on 1/29/2007.

PRIORITY

Priority to US Provisional Application 60/396,908, filed 07/17/2002, has been acknowledged.

OBJECTIONS

Claims 4 and 5 have been amended to correct the grammatical errors, and are now acceptable.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 remain rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. This rejection is reiterated.

According to the revised Guidelines, a claimed invention directed to a statutory process must result in (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. The revised Guidelines also state that the focus is “not on whether the steps taken to achieve a particular result are useful, tangible, and concrete, but rather on whether the final result achieved by the claimed invention is useful, tangible, and concrete.”

The instant claims are directed to a method for “finding translation initiation codons in a nucleotide sequence.” Claim 1 now results in a step of “locating translation initiation codons in said second data set based on the probability calculated in step d).” Thus, the claimed method does not result in a physical transformation of matter, as this claimed result encompasses a non-physical method step that may be practiced inside of a computer (i.e. *locating codons inside of a computer*). Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible

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(i.e. communicated to a user), and useful result (i.e. a specific and substantial). For the above reasons, the instant claims lack a “tangible” result and thus do not recite more than a 35 U.S.C. 101 judicial exception. Therefore, the instant claims are not statutory.

This rejection could be overcome by amending the claims to recite a step wherein the result of the claimed method is communicated to a user (i.e. real world result), graphically displayed, or output (e.g. to a user, to a memory, or to another computer) or by amending the claims to include a step of a physical transformation of matter (e.g. assay). For an updated discussion of statutory considerations, see the revised Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV (Latest Revision August 2006).

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-5 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for finding initiation codons in a nucleotide sequence using Bayes Network construction in Quadratic Discriminant Analysis, does not reasonably provide enablement for finding initiation codons in a nucleotide sequence using a quadratic discriminant function in Quadratic Discriminant Analysis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant's arguments, filed 1/29/2007, that an actual quadratic discriminant function is not necessary for practicing the invention, and that applicant has provided a specific working example wherein various scoring functions and feature variables were used to generate a quadratic discriminant function for finding initiator codons are not persuasive for the following reasons.

Applicant did not distinctly and specifically point to any particular sections of the Specification to support this assertion, nor did applicant address any of the Examiner's contentions as set forth in the previous office action, nor did the applicant specifically point out how the amendments to the instant claims would serve to overcome this rejection. Furthermore, Zhang et al. [p.332, Col. 2], teaches that choosing the set of feature variables that is most discriminative with respect to the classes under investigation is an unpredictable art which depends heavily on the investigator's insight to the nature of the subject. Therefore the Examiner maintains that it would require undue experimentation by one of skill in the art to predictably practice the full scope of the instantly claimed invention. For the above reasons, this rejection is maintained and reiterated to address the amendments to claim 1.

The instant claims are enabled for Bayes analysis in combination with a discriminant function because the instant specification teaches Bayes Network construction [p.15], and exemplifies how to use a Bayes Network for the statistical characterization of initiator or pseudoinitiator codons in a training set to produce parameters [p.39].

In the instant case, the claimed subject matter, drawn to finding initiation codons in a nucleotide sequence, lacks enablement for the following reasons:

Claim 1 has been amended and now recites "using Quadratic Discriminant Analysis with a combination of feature variables that optimally classify ATG triplets in a nucleotide sequence as initiator codons or pseudoinitiator codons based on the numerical score in step b) to

generate a quadratic discriminant function." Given the nature of the invention, finding initiation codons in a nucleotide sequence using Quadratic Discriminant Analysis requires a disclosure of the specific "combinations of features", "scoring functions", and "scoring function parameters" as claimed and as recited in Tables 1, 2, and 3, for generating a quadratic discriminant function as in claim 1. Merely listing Tables comprising variable and class names [p.13, 21, and 31] without a full disclosure for each of these item listed does not provide sufficient guidance. The specification does not provide specific equations for a "quadratic discriminant function" as it relates to all of the claimed parameters and functions required to generate the quadratic discriminant function. Therefore applicants have not made a "full" disclosure of the "quadratic discriminant function" required to practice the claimed subject matter, and have not provided sufficient guidance for "generating a quadratic discriminant function" (instant claim 1, step d). In general, computational methods show a range of accuracies for the prediction of coding and intron regions within large regions of uncharacterized genomic DNA at the nucleotide level, with an average fraction of actual exon identification of less than 50% [Zhang et al.]. Despite the high level of skill in the art, one skilled in the art would not know how to determine translation initiation codons in a nucleotide sequence using a quadratic discriminant analysis without knowledge of a specific quadratic discriminant function as it relates to the specific design parameters, therefore it would require undue experimentation by one of skill in the art to predictably practice the full scope of the instantly claimed invention. [Wands factors (1), (2), (4), (5), (6), (7), (8)].

WRITTEN DESCRIPTION

Claim 1-5 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

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in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments that sufficient written description was provided in the specification are not persuasive for the reasons set forth above. This rejection is maintained and reiterated to address the amendments to claim 1.

Claim 1 has been amended and now recites "using Quadratic Discriminant Analysis with a combination of feature variables that optimally classify ATG triplets in a nucleotide sequence as initiator codons or pseudoinitiator codons based on the numerical score in step b) to generate a quadratic discriminant function." For the above reasons, and for the reasons set forth in the previous office action mailed 05/18/2006, the Examiner maintains that neither the instant claims nor the specification provides a written description for generating a quadratic discriminant function derived for use with the associated optimally selected design parameters (i.e. output of said scoring functions). Therefore, the description lacks sufficient detail as to actual quadratic discriminant function used in the Quadratic Discriminant Analysis, such that one of skill in the art would have been aware that applicants were actually in possession of such a function at the time of invention.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2-5 are rejected as they depend directly from claim 1.

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Claim 1 (step c) now recites "using Quadratic Discriminant Analysis with a combination of feature variables that optimally classify ATG triplets in a nucleotide sequence as initiator codons or pseudoinitiator codons based on the numerical score in step b) to generate a quadratic discriminant function:" It is well known that QDA is a statistical method for calculation. Therefore, it is unclear as to the intended meaning of "using quadratic discriminant analysis" to "generate a quadratic discriminant function." Clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being made obvious by Salamov et al. (Bioinformatics, 1998, Vol. 1, No. 5, p.384-390), in view of Zhang et al. (Proc. Natl. Acad. Sci., 1997, Vol. 94, p.565-568, as filed in the IDS). *This rejection is necessitated by amendment.*

Salamov et al. teach a method for finding translation initiation codons in a nucleotide sequence [Abstract]. More specifically, Salamov et al. teach the following aspects of the instantly claimed invention:

- Obtaining a “positive” data set comprising real ATG start codons and other false ATG nucleotides (i.e. pseudoinitiator codons) and a “negative” (i.e. control) data set that includes regions after the initiator codon [p.386, Col. 2, ¶ 3]
- Defining six characteristics (i.e. features) of initiator codons [p.386, Col. 2, ¶ 5 – p.387, Col. 2, ¶ 2], which include scoring functions and parameters used to analyze sequence position data around each ATG region [p.387, Section (1)], and positional weight scoring functions to quantify resemblance of ATG triplets to initiator codons [p.387, Col. 1, Section (5)], as in claim 1, step b).
- Using LDA to determine the probability that each ATG in the positive data set (i.e. first data set) is an initiator codon based on determining the top scoring ATGs from each sequence [Fig. 2(a)], as in claim 1, step c).
- Using LDA to determine the probability that each ATG lying above a threshold in the negative data set (i.e. second data set) is a true initiator codon [Fig. 2(b)], as in claim 1, step d) and e)].
- Combinations of features comprising frequency of codon initiators, frequency of coding and non-coding regions (i.e. codon usage) around each ATG from –14 to +5, and in-frame hexanucleotide composition (i.e. in frame hexamer composition) [p.388, Sections (1) and (2)], as in claim 2 (Table 1).
- Scoring functions directed to upstream ATG scores (i.e. Upstream Codon Score) [p.388, Section (5)], and measure of accuracy scores (i.e. Score) [p.388, Col. 2], as in claim 3 (Table 2).

Salamov et al. do not specifically teach the use of “quadratic determinant analysis” for finding translation codons in a nucleotide sequence, as in claim 1.

Zhang et al. teach the identification of protein coding regions in nucleotide sequences using quadratic discriminant analysis (QDA) [Abstract]. Zhang et al. also teach data analysis of first and second data sets (i.e. exons and pseudo-exons) using a combination of nine feature variables (e.g. x1, x2, ..., x9), calculation of performance measures using Bayes theorem [p.566, Col. 2, ¶ 1], and correlations coefficients greater than 0.8 [Table 2 and 3], as in claims 1, 4, and 5. Zhang et al. do not specifically teach feature variable names as recited in claims 4 and 5 (Table 3). However, Zhang et al. clearly teaches feature variables for frame-specificity (e.g. x7), frequency (e.g. x2) over a plurality of different windows, and codons (e.g. x1), as well as variables for data correlation (CC), as in claims 4 and 5. As no “feature variables”, equations, or functions are recited in the claims that would serve to illustrate in what way “any combination of feature variables provided in Table 3 wherein the combination comprises one feature variable from each of any two feature variable classes,” as recited in claims 4 and 5, the Examiner has broadly interpreted this limitation to encompass the teachings of Zhang et al.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the method of finding translation initiation codons as taught by Salamov et al. using the QDA technique of Zhang et al., as QDA is well known as a direct extension of classic linear discriminant analysis [Zhang et al., p.565, Col. 2]. One of ordinary skill in the art would have been motivated to combine the above teachings to use a well known technique for improving data classification in predictive models [Zhang et al., p.565, Col. 2], resulting in the practice of the instant claimed invention with a reasonable expectation of success.

CONCLUSION

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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